

In re Application of: Giora AMITZUR et al  
 Serial No.: 10/537,913  
 Filed: December 6, 2005  
 Office Action Mailing Date: February 6, 2007

Examiner: Zoe E. Baxter  
 Group Art Unit: 3735  
 Attorney Docket: 30028

**In the Claims:**

WHAT IS CLAIMED IS:

1. (Currently Amended) A method of determining endothelial dependent vasoactivity of a subject, the method comprising:

recording pressure-related signals of a plurality of locations adjacent to at least one blood vessel;

extracting ~~at least one~~ parameters from said pressure-related signals, said parameters comprise a first parameter, sensitive to arterial radius changes at the initial stage of arterial dilatation, and a second parameter, sensitive to arterial radius changes at larger arterial dilatation; and

using said ~~at least one~~ parameters to determine a change of at least one characteristic of said at least one blood vessel, said change being representative of endothelial functioning;

~~thereby~~ determining the endothelial dependent vasoactivity of the subject using said parameters; and

displaying at least an indication of said endothelial dependent vasoactivity.

2. (Original) The method of claim 1, further comprising determining an autonomic nervous system activity of the subject.

3. (Original) The method of claim 1, further comprising stimulating said at least one blood vessel.



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4. (Original)            The method of claim 3, wherein said stimulating of said at least one blood vessel is effected by a procedure selected from the group consisting of a mechanical stimulation, a thermal stimulation a chemical stimulation, an electrical stimulation a mental stress stimulation and a physical exercise stimulation.

5. (Currently Amended)        The method of claim 3, wherein said stimulating of said at least one blood vessel ~~is~~ bycomprises applying external pressure on said at least one blood vessel.

6. (Currently Amended)        The method of claim 3, wherein said stimulating of said at least one blood vessel ~~is~~ bycomprises reducing a temperature of said at least one blood vessel.

7. (Original)            The method of claim 1, wherein said at least one blood vessel is selected from the group consisting of a brachial artery, a radial artery and a carotid artery.

8. (Original)            The method of claim 2, further comprising correlating said endothelial functioning and said autonomic nervous system activity, so as to obtain a correlation function, and using said correlation function to at least preliminarily determine the endothelial dependent vasoactivity of the subject.

9. (Currently Amended)        The method of claim 2, wherein said determining of said autonomic nervous system activity ~~is~~ bycomprises heart rate variability analysis of said pressure-related signals.



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10. (Original)            The method of claim 2, wherein said determining of said autonomic nervous system activity comprises recording electrocardiogram signals of a chest of the subject and performing heart rate variability analysis of said electrocardiogram signals, thereby determining said autonomic nervous system activity.

11. (Original)            The method of claim 10, further comprising determining a pre-ejection period and valve-artery period.

12. (Original)            The method of claim 11, wherein said valve of said valve-artery period is an aortic valve and said artery of said valve-artery period is a carotid artery.

13. (Original)            The method of claim 11, wherein said determination of said pre-ejection period and said valve-artery period, comprises determining an elapsed time between peaks of said electrocardiogram signals and peaks of said pressure-related signals.

14. (Original)            The method of claim 13, wherein said peaks of said electrocardiogram signals comprise QRS peaks.

15. (Currently Amended)    The method of claim 1, wherein said recording of said pressure-related signals ~~is by~~comprises piezoelectric ceramic elements. |

16. (Currently Amended)    The method of claim 1, wherein said recording of said pressure-related signals ~~is by~~comprises a membrane-based sensor. |



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17. (Original)            The method of claim 16, wherein said membrane-based sensor is an electrate microphone.

18. (Original)            The method of claim 1, further comprising obtaining a frequency decomposition of said at least one parameter, and using said frequency decomposition for determining the endothelial dependent vasoactivity of the subject.

19. (Original)            The method of claim 1, wherein said at least one parameter is selected from the group consisting of an amplitude of said pressure-related signals, a width of said pressure-related signals and an elapsed time between two peaks of said pressure-related signals.

20. (Original)            The method of claim 19, further comprising obtaining a frequency decomposition of said amplitude, and using said frequency decomposition for determining the endothelial dependent vasoactivity of the subject.

21. (Original)            The method of claim 19, further comprising obtaining a frequency decomposition of said width, and using said frequency decomposition for determining the endothelial dependent vasoactivity of the subject.

22. (Original)            The method of claim 19, further comprising obtaining a frequency decomposition of said elapsed time, and using said frequency decomposition for determining the endothelial dependent vasoactivity of the subject.



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23. (Original)           The method of claim 10, wherein said at least one parameter is selected from the group consisting of an amplitude of said pressure-related signals, a width of said pressure-related signals, an elapsed time between two peaks of said pressure-related signals and an elapsed time between peaks of said electrocardiogram signals and peaks of said pressure-related signals.

24. (Original)           The method of claim 1, wherein said at least one characteristic of said at least one blood vessel is selected from the group consisting of a radius of said at least one blood vessel and an elastic modulus of said at least one blood vessel.

25. (Original)           The method of claim 1, wherein said extracting of said at least one parameter comprises:

- (a) scanning pressure-related signals recorded of a first location and detecting a first peak;
- (b) scanning pressure-related signals recorded of a second location and detecting a second peak corresponding to said first peak;
- (c) measuring an elapsed time between said first peak and said second peak; and
- (d) repeating said steps (a)-(c) at least once.



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26. (Currently Amended) A system for determining endothelial dependent vasoactivity of a subject, the system comprising:

an arrangement of sensors for recording pressure-related signals of a plurality of locations adjacent to at least one blood vessel;

a processing unit operable to receive, record and process said pressure-related signals and configured to display results of said processing;

said processing unit being designed and programmed to extract ~~at least one~~ parameters from said pressure-related signals, and to use said ~~at least one~~ parameters to determine a change of at least one characteristic of said at least one blood vessel, said change being representative of endothelial functioning, wherein the parameters extracted from the pressure-related signals comprise a first parameter, sensitive to arterial radius changes at the initial stage of arterial dilatation, and a second parameter, sensitive to arterial radius changes at larger arterial dilatation.

27. (Original) The system of claim 26, further comprising electronic-calculation functionality for determining an autonomic nervous system activity of the subject.

28. (Original) The system of claim 26, further comprising a mechanism for stimulating said at least one blood vessel.

29. (Original) The system of claim 28, wherein said mechanism for stimulating said at least one blood vessel is selected from the group consisting of a mechanical mechanism, a thermal mechanism, a chemical mechanism an electrical mechanism, a mechanism for generating mental stress and a device for allowing the subject to perform physical exercise.



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30. (Original) The system of claim 28, wherein said mechanism is operable to apply external pressure on said at least one blood vessel.

31. (Original) The system of claim 30, wherein said mechanism comprises a sphingomanometer.

32. (Original) The system of claim 28, wherein said mechanism is operable to reduce a temperature of said at least one blood vessel.

33. (Original) The system of claim 32, wherein said mechanism is selected from the group consisting of a bath of fluid and a cuff of fluid, said fluid being at a predetermined temperature.

34. (Original) The system of claim 26, wherein said at least one blood vessel is selected from the group consisting of a brachial artery, a radial artery and a carotid artery.

35. (Original) The system of claim 27, wherein said processing unit is operable to calculate heart rate variability from said pressure-related signals thereby to determine said autonomic nervous system activity.

36. (Currently Amended) The system of claim 27, further comprising at least one electrocardiogram lead, ~~designed connectable to a chest of the subject.~~



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37. (Original)           The system of claim 36, wherein said processing unit is operable to calculate heart rate variability from electrocardiogram signals sensed by said at least one electrocardiogram lead, thereby to determine said autonomic nervous system activity.

38. (Currently Amended)   The system of claim 26, wherein said sensors ~~are~~ comprise at least one piezoelectric ceramic elements.

39. (Currently Amended)   The system of claim 26, wherein said sensors comprise at least one membrane-based ~~are~~ sensors.

40. (Currently Amended)   The system of claim 39, wherein said sensors ~~are~~ comprise at least one electrate microphones.

41. (Original)           The system of claim 26, further comprising a spectral analyzer for analyzing said at least one parameter and obtaining a frequency decomposition of said at least one parameter, said frequency decomposition being representative of the endothelial dependent vasoactivity of the subject.

42. (Original)           The system of claim 26, wherein said at least one parameter is selected from the group consisting of an amplitude of said pressure-related signals, a width of said pressure-related signals and an elapsed time between two peaks of said pressure-related signals.



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43. (Original) The system of claim 36, wherein said at least one parameter is selected from the group consisting of an amplitude of said pressure-related signals, a width of said pressure-related signals, an elapsed time between two peaks of said pressure-related signals and an elapsed time between peaks of electrocardiogram signals and peaks of said pressure-related signals.

44. (Original) The system of claim 26, wherein said at least one characteristic of said at least one blood vessel is selected from the group consisting of a radius of said at least one blood vessel and an elastic modulus of said at least one blood vessel.

45. (Currently Amended) A method of determining endothelial dependent vasoactivity of a subject, the method comprising:

- (a) applying a first stimulus to at least one blood vessel;
- (b) measuring a pulse wave velocity of blood flowing in said at least one blood vessel;
- (c) determining an autonomic nervous system activity of the subject;
- (d) correlating said pulse wave velocity and said autonomic nervous system activity, so as to obtain a correlation function having an index; ~~and~~
- (e) if said index has a predetermined value then:
  - (i) applying a second stimulus on said at least one blood vessel; and
  - (ii) repeating said steps (b)-(c); and
- thereby determining the endothelial dependent vasoactivity of the subject; and
- (f) displaying at least an indication of the endothelial dependent vasoactivity of the subject.



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46. (Original) The method of claim 45, wherein said step (e) further comprises applying said second stimulus on at least one additional blood vessel and repeating said steps (b)-(c) for said at least one additional blood vessel.

47. (Original) The method of claim 45, wherein said first and said second stimuli are each independently selected from the group consisting of a stimulus, a thermal stimulus, a chemical stimulus, an electrical stimulus, a mental stress stimulus and a physical exercise stimulus.

48. (Original) The method of claim 45, wherein said stimulus comprises external pressure.

49. (Original) The method of claim 45, wherein said stimulus comprises temperature reduction.

50. (Original) The method of claim 45, wherein said at least one blood vessel is selected from the group consisting of a brachial artery, a radial artery and a carotid artery.

51. (Original) The method of claim 46, wherein said at least one additional blood vessel is selected from the group consisting of a brachial artery, a radial artery and a carotid artery.

52. (Currently Amended) The method of claim 45, wherein said determining of said autonomic nervous system activity ~~is by~~comprises heart rate variability analysis of said pressure-related signals.

53. (Original) The method of claim 45, wherein said determining of said autonomic nervous system activity comprises recording electrocardiogram signals



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of a chest of the subject and performing heart rate variability analysis of said electrocardiogram signals, thereby determining said autonomic nervous system activity.

54. (Currently Amended) The method of claim 45, wherein said measuring a pulse wave velocity ~~is~~ bycomprises recording pressure-related signals using piezoelectric ceramic elements.

55. (Currently Amended) The method of claim 45, wherein said wherein said measuring a pulse wave velocity ~~is~~ bycomprises recording pressure-related signals using a membrane-based sensor.

56. (New) The system of claim 26, wherein said first parameter is an amplitude of a pressure related signal.

57. (New) The system of claim 26, wherein said second parameter is an elapsed time between peaks of a pressure related signal and an ECG signal.

58. (New) The method of claim 1, wherein said first parameter is an amplitude of a pressure related signal.

59. (New) The method of claim 1, wherein said second parameter is an elapsed time between peaks of a pressure related signal and an ECG signal.

60. (New) The system of claim 36, wherein said cardioelectrogram lead is designed to be connectable to a chest of the subject.